88 Diarrhea

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Definition

Diarrhea is an increase in the volume and weight of daily stool. The frequency of bowel movements is usually increased as well.

Technique

Diarrhea may mean many things to different people. A patient's subjective experience of altered bowel habits may not necessarily fit the physician's criteria for diarrhea. For some patients, the occurrence of a single unformed stool is enough to provoke a visit to the physician for "diarrhea." Thus it is important for the physician first to determine if the patient has diarrhea and then proceed to characterize it.

The first question to be asked is, "How have your normal bowel habits changed?" Allowing the patient to speak spontaneously, one should be listening for important historical factors, as listed in Table 88.1.

The frequency and size of each bowel movement are important. Small and frequent bowel movements often indicate left colon or rectal disease, whereas voluminous stools usually indicate small bowel or right colon disease. Do the symptoms interrupt normal sleeping patterns? The absence of nocturnal diarrhea is suggestive of functional bowel disease. Are the symptoms acute, that is, of less than 7 to 10 days' duration or chronic?

Attempt to elicit a description of the stool: What are your abnormal bowel movements like? Are the stools formed, soft or watery? Is any blood or mucus present? Is there ever any undigested food or fat in the stool? Is the quantity or character of the stool affected by fasting or certain foods? The color of the stool is rarely helpful diagnostically unless melena is present or the stools are acholic.

Next, inquire about any medications that might cause diarrhea, such as antacids, laxatives, antibiotics, or colchicine. Any recent travel, a history of possible exposure to tainted foods or diarrheal illness in the family, and a sexual history are also important.

Ask about associated symptoms, both those related to the gastrointestinal tract (e.g., abdominal pain, cramping, nausea, vomiting, rectal urgency, incontinence, bloating, increased flatus or jaundice), and more constitutional symptoms (e.g., fever, chills, malaise, anorexia, or weight loss).

Finally, a review of systems may point out some important related involvement that can serve as a clue to diagnosis, for example, arthritis or skin rash associated with inflammatory bowel disease or anxiety associated with irritable bowel disease.

Table 88.1
Diarrhea: Important Historical Features

Frequency of stool
Volume and quantity of stools
Time of occurrence—night or day
Duration of symptoms
Nature of stools
Presence of blood or mucous
Consistency of stool
Presence of fat or undigested foods
Color of stools
Drug history
Travel history
Recent food history
Exposure history within family or workplace
Sexual history
Associated gastrointestinal symptoms
Pain, nausea, vomiting, jaundice
Systemic symptoms
Fever, chills, weight loss, anorexia, arthritis

Basic Science

To understand better what causes diarrhea and how to treat it, one must first have an understanding of the normal digestive system. Approximately 2 liters are ingested daily in the normal diet. By the time this food material has reached the proximal duodenum, another 7 liters of digestive secretions from the stomach, liver, pancreas, intestine, and salivary glands have been added. As this chyme is passed along the small intestine, the osmolality is adjusted so that, at the distal ileum, the bowel contents are isotonic with plasma and total only 1 to 2 liters.

The colon absorbs much of the remaining fluid, leaving approximately 100 to 150 cc of slightly hypertonic stool to be excreted. The colon has the capacity to absorb up to about 4 liters per day, but normally one's excretory patterns prevent complete desiccation of the bowel movement.

Diarrhea results when there is alteration of this normal physiologic process of digestion and absorption. There are multiple causes for diarrhea and there may be multiple pathophysiologic mechanisms for a single disease entity. Nonetheless, the following pathophysiologic classification provides a useful framework for approaching diarrhea:

- Diarrhea secondary to altered mucosal transport or secretory dysfunction
- Osmotic diarrhea
- Diarrhea secondary to malabsorption
- Exudative diarrhea
- Diarrhea secondary to altered bowel motility

Diarrhea Secondary to Altered Mucosal Transport or Secretory Dysfunction

Along the small bowel both absorption and secretion of fluid and electrolytes occur; normally there is net absorption.

Diarrhea can result when either decreased absorption or increased secretion occurs.

Classic secretory diarrhea is caused most commonly by toxins produced by various bacterial pathogens such as *Staphylococcus, Escherichia coli,* and *Vibrio cholerae.* Certain hormones, when produced in excess, such as vasoactive intestinal peptide (VIP) and gastrin produced by pancreatic tumors, and calcitonin produced by medullary cancer of the thyroid, can also stimulate excessive mucosal secretion, leading to diarrhea.

In the case of cholera and VIP tumors, this loss of net absorption across the intestinal mucosa is thought to be mediated by an increased concentration of certain mucosal cell cyclic nucleotides. Experimental evidence suggests that elevated levels of cyclic AMP can stimulate net anion secretion, thus causing diarrhea.

Secretory diarrhea occurs independent of dietary intake and does not subside with fasting. In addition, there is no significant stool osmotic gap, defined as:

$$\text{Measured fecal osmolality} = 2(\text{Na} + \text{K})\ \text{stool}.$$

In other words, the stool osmolality is determined solely by measurable electrolytes and not by some nonabsorbed solute, as is found in osmotic diarrhea, discussed next.

Osmotic Diarrhea

Osmotic diarrhea results from the presence of osmotically active, poorly absorbed solutes in the bowel lumen that inhibit normal water and electrolyte absorption. Certain laxatives such as lactulose and citrate of magnesia or maldigestion of certain food substances such as milk are common causes of osmotic diarrhea. An increased osmotic load can be measured in the stool. This type of diarrhea ceases with fasting.

Diarrhea Secondary to Malabsorption

Numerous pathologic conditions including pancreatic insufficiency, biliary disease, Crohn's disease, intestinal lymphangiectasia, and celiac disease can cause malabsorption. For several of these malabsorption syndromes, more than one pathophysiologic mechanism is responsible for the diarrhea, making a simple classification system difficult. Nonetheless, some general points can be made.

The increase in stool volume secondary to fatty acid malabsorption results directly from the presence of large quantities of unabsorbed fat in the stool (i.e. steatorrhea). By excluding or modifying fat intake, this form of diarrhea often resolves.

When bile salts are malabsorbed, such as occurs in disease of the terminal ileum, they are deconjugated by colonic bacteria to bile acids that directly stimulate colonic mucosal secretion, causing more diarrhea.

Malabsorption and diarrhea can also occur as a result of direct loss of absorptive surface either by surgical resection of the bowel or by atrophy of the small bowel villous border, as seen in celiac disease. If an enteroenteric fistula is present, as may occur in Crohn's disease, whole sections of intestinal absorptive surface can be bypassed.

Exudative Diarrhea

Diseases associated with large quantities of inflammatory exudate, that is, blood, pus, and proteinaceous material, can produce diarrhea. These inflammatory products in themselves cause increased stool volume and frequency, but altered absorption of fluid and electrolytes also plays an important role. Mucosal inflammation can occur with diverticulitis, inflammatory bowel disease, or invasive enteric infections such as shigella, salmonella, or campylobacter. The etiology for the inflammatory response in ulcerative colitis and Crohn's disease remains poorly understood.

Diarrhea Secondary to Altered Bowel Motility

When intestinal transport is delayed in the small bowel, as with scleroderma or blind loop syndromes, the resultant bowel stasis encourages bacterial overgrowth and subsequent bile salt deconjugation. Diarrhea is then the direct result of fat malabsorption and increased colonic secretion.

In contrast, significant increases in bowel motility can deliver excessively large volumes of stool to the colon. Diarrhea can result when the maximum colonic absorptive capacity of 4 liters a day is exceeded. Also, an alteration in colonic motility such that bowel contents are emptied before adequate absorption can occur has been offered as a possible explanation for the diarrhea associated with irritable bowel disease.

Clinical Significance

Diarrhea is a very common complaint of outpatients and not infrequently, a problem among hospitalized patients. After a careful history and physical examination, a differential diagnosis must be formulated so that realistic decisions regarding further evaluation and treatment can be made. One must always be certain not to miss an acute abdominal process such as ischemic colitis.

Acute Diarrhea

Clinically it is most useful to divide diarrhea into acute versus chronic illness. Acute diarrhea is primarily caused by infectious agents, toxins, and drugs. Viral gastroenteritis is one of the most common causes. The Norwalk agent, a parvovirus, and rotaviruses are the viral agents isolated most frequently. There is some evidence to suggest that a pathologic alteration of the small bowel mucosa adversely affects absorption of luminal contents.

Toxins produced by bacteria are also frequent causes of acute diarrhea. Staphylococcal food poisoning is a prime example. Because the etiologic agent is a preformed toxin, the illness is characterized by abrupt onset of nausea, vomiting, and diarrhea. By contrast, in *Clostridium perfringens* infection, the onset of diarrhea is delayed because the production of the responsible toxin requires bacterial replication. *Bacillus cereus* produces two toxins: a preformed one that causes an illness similar to staphylococcal food poisoning and one more like that seen with *C. perfringens* infections.

The presence of blood or mucus in the diarrhea, along with systemic symptoms of fever, chills, and abdominal pain, suggests infection with an invasive organism such as shigella, salmonella, campylobacter, or yersinia. The symptoms are related to mucosal damage or irritation. Fecal leukocytes are commonly seen on stool smear.

A food history may provide a clue to the infectious agent. For example, *B. cereus* is associated with ingestion of fried rice, *Vibrio parahemolyticus* with shellfish, yersinia with milk,

and salmonella with poultry. Similarly, a travel history is important. Enterotoxigenic *E. coli* has been isolated in travelers to Mexico and other Central and South American countries. Giardiasis has been shown to be endemic in Leningrad and in remote areas of the western United States. These emporiatric infections are thought to be related to contaminated water used either for drinking or washing foods.

Homosexual men are predisposed to enteric infections associated with diarrhea—the so-called gay bowel syndrome. Entamoeba histolytica, Giardia, Cryptosporidia, Campylobacter, Shigella, Chlamydia, Herpes, and Cytomegalovirus infections have all been described in these patients. Indeed, these infections may be harbingers of the acquired immunodeficiency syndrome (AIDS).

Certain medications, particularly antibiotics, can cause a *Clostridium difficile* enterocolitis, or pseudomembranous colitis. This can occur up to several weeks after antibiotic therapy. Multiple antibiotics have been implicated in this syndrome, but the ones most frequently identified are clindamycin, cephalosporins, and ampicillin.

Inflammatory bowel disease such as Crohn's disease or ulcerative colitis can also cause acute diarrhea associated with systemic symptoms, but those illnesses are more often associated with chronic diarrhea. In *chronic or recurrent diarrhea,* the diarrhea has usually persisted beyond 10 to 14 days. This observation often rules out many of the infectious or toxigenic diarrheas listed above because they are usually self-limited or readily treated. Infections such as giardiasis or amebiasis, however, may be difficult to diagnose and may present as chronic diarrhea.

A number of humorally mediated chronic diarrheal syndromes deserve mention, although they are rare. These hormones are produced by autonomously functioning tumors, and all cause a chronic voluminous secretory diarrhea. The diarrhea is characterized by its persistence in a fasting state and a normal stool osmotic gap. Both gastrin and vasoactive intestinal peptide (VIP) have been isolated from islet cell tumors of the pancreas.

In patients with the *Zollinger–Ellison syndrome* (gastrinoma), the hypergastrinemia produces diarrhea by overwhelming the bowel with gastric secretions, as well as by acid inactivation of pancreatic enzymes.

Pancreatic cholera, or the WDHA (watery diarrhea, hypokalemia, and achlorhydria) syndrome, results from production of VIP, which appears to activate intestinal adenylate cyclase that stimulates excessive secretions with resultant diarrhea. Hypokalemia, hypercalcemia, and metabolic acidosis are common sequelae.

Secretory diarrhea is also associated with hormones such as increased secretion of serotonin in carcinoid, calcitonin in medullary thyroid carcinoma, and a not fully identified substance produced by tumors of the sympathetic nervous system. In addition to stimulating intestinal secretion, serotonin also increases bowel motility, which contributes to the diarrhea associated with the malignant carcinoid syndrome. Patients with hyperthyroidism also have increased bowel motility, and diarrhea is not an uncommon presenting complaint.

There are multiple causes for chronic or recurrent diarrhea. Once again, the history and physical examination are crucial to diagnosis, but more often than not, invasive studies are needed in order to make the diagnosis. It is often helpful to determine whether the patient is having small or large volumes of stool. Patients with voluminous diarrhea often have disease of the upper intestinal tract—usually secondary to either an osmotic or secretory process. Patients with small-volume diarrhea often have disease in their left colon or rectum, often an inflammatory process. But probably the most common cause for intermittent small-volume chronic diarrhea is the *irritable bowel syndrome,* which is always a diagnosis of exclusion. Patients often report alternating diarrhea and constipation associated with abdominal distention; relief is obtained with defecation. Of note, there is usually a normal 24-hour stool volume despite increased frequency of bowel movements. The cause of the irritable bowel syndrome is unknown, although some investigators believe it is related to altered colonic motility.

Another cause of intermittent chronic diarrhea is *laxative abuse.* This is one of the most common causes of diarrhea in patients in whom the diagnosis has remained elusive despite extensive evaluation. Indeed, in some cases, the diagnosis has been made only after a search of the patient's room.

Drugs that can cause chronic diarrhea include quinidine, colchicine, sorbitol, and cytotoxic agents.

Chronic diarrhea is also associated with diseases affecting the absorptive surfaces of the bowel, such as celiac disease, radiation enteritis, bowel ischemia, and inflammatory bowel disease. Celiac disease is characterized by direct loss of the villous border of the intestinal mucosa with resultant malabsorption. Radiation treatment for abdominal or pelvic malignancies or bowel ischemia inevitably produces mucosal damage that can cause chronic diarrhea. In Crohn's disease or ulcerative colitis, inflammatory exudate contributes to the diarrhea, but malabsorption from inflammatory involvement of absorptive surfaces is sometimes an important factor as well.

Miscellaneous Causes

Other processes that can affect absorption include specific enzyme deficiencies. In *pancreatic insufficiency* there is impaired lipolysis secondary to a deficiency in lipase, which can result in severe steatorrhea and diarrhea. One of the most common enzyme deficiencies is *lactase deficiency,* found most commonly in blacks, Asians, American Indians, and a small percentage of northern Europeans. This enzyme breaks down nonabsorbable lactose, a sugar found in milk and dairy products, into readily absorbable glucose and galactose. In the absence of this enzyme, colonic bacteria metabolize the lactose and produce great quantities of gas. Patients complain of abdominal bloating and cramping as well as diarrhea. The symptoms resolve when these lactose-rich foods are avoided or when the lactose is predigested before ingestion.

Colonic polyps and tumors may present with diarrhea either because of abnormal secretory function, as may occur with villous adenomas, or because of partial obstruction. Partial obstruction results in diarrhea when there is an overflow of liquid stool around the obstruction. Stool impaction in an elderly patient may cause partial obstruction with resultant overflow incontinence as well.

Finally, patients often complain of diarrhea when the problem is an *abnormality of anal sphincter tone.* These patients are often incontinent and, in fact, their stool volume is normal.

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